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Genomic sequencing of human chromosome 19 and DNA repair genes.

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To provide resources for future functional studies, we have focused our sequencing efforts on two areas: genomic regions containing DNA repair genes and human chromosome 19. Utilizing a high-resolution, bacterial clone-based map of human chromosome 19, we have generated over 1.8 Mb of genomic sequence targeted to selected regions of biological interest. This chromosome is GC-rich (and thus, potentially gene-rich) and contains a large number of clustered gene families, several of which are targets for genomic sequencing. These include several zinc finger (ZNF) and olfactory receptor genes clusters in 19q13.4 and 19p13.1, respectively. Sequence analysis of a variety of regions from chromosome 19 indicate that it is indeed gene-rich, even in regions expected to be gene-poor due to a paucity of genetic markers. For example, analysis of a 100 kb segment of a repeated genomic region (D19S11) in 19p13.1 uncovered a previously unidentified cluster of CYP4F- family genes. Similarly, an ~110 kbp contig containing the RAD23A DNA repair gene in 19p13.2 contains 7 genes, only two of which were known to map to 19. Currently, our largest contiguous target is an ~1 Mb region of 19q13.1 flanked by the genetic markers D19S208 and CANPS. Sequence analysis of 22 cosmids in this contig identified at least 27 new genes, 7 of which appear to be novel, as well as at least 6 genes (APLP1, ATP4A, CD22, MAG, COX6B and CANPS) which had been previously mapped to this interval.

An additional 820 kb of sequence has been targeted to genomic regions containing seven different human and/or mouse DNA repair genes. Comparative analyses have been performed for human and mouse XRCC1, ERCC2, and are underway for XRCC2 and ERCC4.

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